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Review

Pre-surgical mapping of eloquent cortex for paediatric epilepsy surgery candidates: Evidence from a review of advanced functional neuroimaging

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ABSTRACT

Purpose: A review of all published evidence for mapping eloquent (motor, language and memory) cortex using advanced functional neuroimaging (functional magnetic resonance imaging [fMRI] and magnetoencephalography [MEG]) for paediatric epilepsy surgery candidates has not been conducted previously. Research in this area has predominantly been in adult populations and applicability of these techniques to paediatric populations is less established.
Methods: A review was performed using an advanced systematic search and retrieval of all published papers examining the use of functional neuroimaging for paediatric epilepsy surgery candidates.
Results: Of the 2724 papers retrieved, 34 met the inclusion criteria. Total paediatric participants identified were 353 with an age range of 5 months-19 years. Sample sizes and comparisons with alternative investigations to validate techniques are small and variable paradigms are used. Sensitivity 0.72 (95% CI 0.52–0.86) and specificity 0.60 (95% CI 0.35–0.92) values with a Positive Predictive Value of 74% (95% CI 61–87) and a Negative Predictive Value of 65% (95% CI 52–78) for fMRI language lateralisation with validation, were obtained. Retrieved studies indicate evidence that both fMRI and MEG are able to provide information lateralising and localising motor and language functions.
Conclusions: A striking finding of the review is the paucity of studies (n = 34) focusing on the paediatric epilepsy surgery population. For children, it remains unclear which language and memory paradigms produce optimal activation and how these should be quantified in a statistically robust manner. Consensus needs to be achieved for statistical analyses and the uniformity and yield of language, motor and memory paradigms. Larger scale studies are required to produce patient series data which clinicians may refer to interpret results objectively. If functional imaging techniques are to be the viable alternative for pre-surgical mapping of eloquent cortex for children, paradigms and analyses demonstrating concordance with independent measures must be developed.

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1. Introduction

Paediatric epilepsies are the most common serious neurological disorders of childhood, affecting between 0.5-1% of children and young people under the age of 16 years [1]. Childhood epilepsies are associated with the greatest amount of psychological and psychiatric morbidity with psychopathology three-to-six times greater than in the general childhood population [2]. Epilepsies are known to impair behaviour, affect, cognition and learning significantly [2–5]. Not all epilepsies respond to anti-epileptic drugs and other treatments such as the ketogenic diet, vagal nerve stimulators and resective and functional surgery have become available [6–8].

Epidemiological studies indicate that 27 in every million children might benefit from resective surgery for an epilepsy. While this equates to approximately 405 children per year in the UK; only about 25% of such procedures actually take place [9]. An epilepsy in adulthood may lead to detriment to already acquired functions. However, for a child, language, memory and motor functioning are acquired progressively and seizures interfere with what is to be developed, as well as what has been acquired [10]. The International League Against Epilepsy (ILAE) recommends resective surgery is considered for medically refractory epilepsies where a patient has not responded to two or three anti-epileptic drugs or where seizure activity is disabling [9]. The primary aim of resective surgery is seizure freedom although this is not always achieved. The likelihood of seizure freedom is related to the aetiology of the epilepsy and extent of the procedure undertaken [9]. For instance, surgery in the event of developmental malformations such as hemimegalencephaly has been associated with reduced likelihood of complete seizure freedom in comparison to other malformations [11]. Secondary to seizure control are outcomes for cognition and behaviour [12] with seizure freedom or reduction being associated with measured reductions in psychopathology and aggressive behaviours [13].

Surgical candidacy has traditionally been established via semiology, structural neuroimaging, vEEG and neuropsychological evaluation [9,14]. These remain essential investigations. The purpose of epilepsy surgery is to abolish or significantly reduce epileptic seizures that are refractory to medication. However, the extent of resection is limited by the potential for cognitive, perceptual and motor deficits [15]. The mapping of eloquent areas for language, memory and motor function is critical for refractory epilepsies. Despite its reported limitations, the intracarotid amobarbital test or Wada continues to be used to estimate potential post-operative impairment to language and memory [15,16]. As a demanding and invasive test, Wada has risks and it serves to lateralise and not localise function. Significant

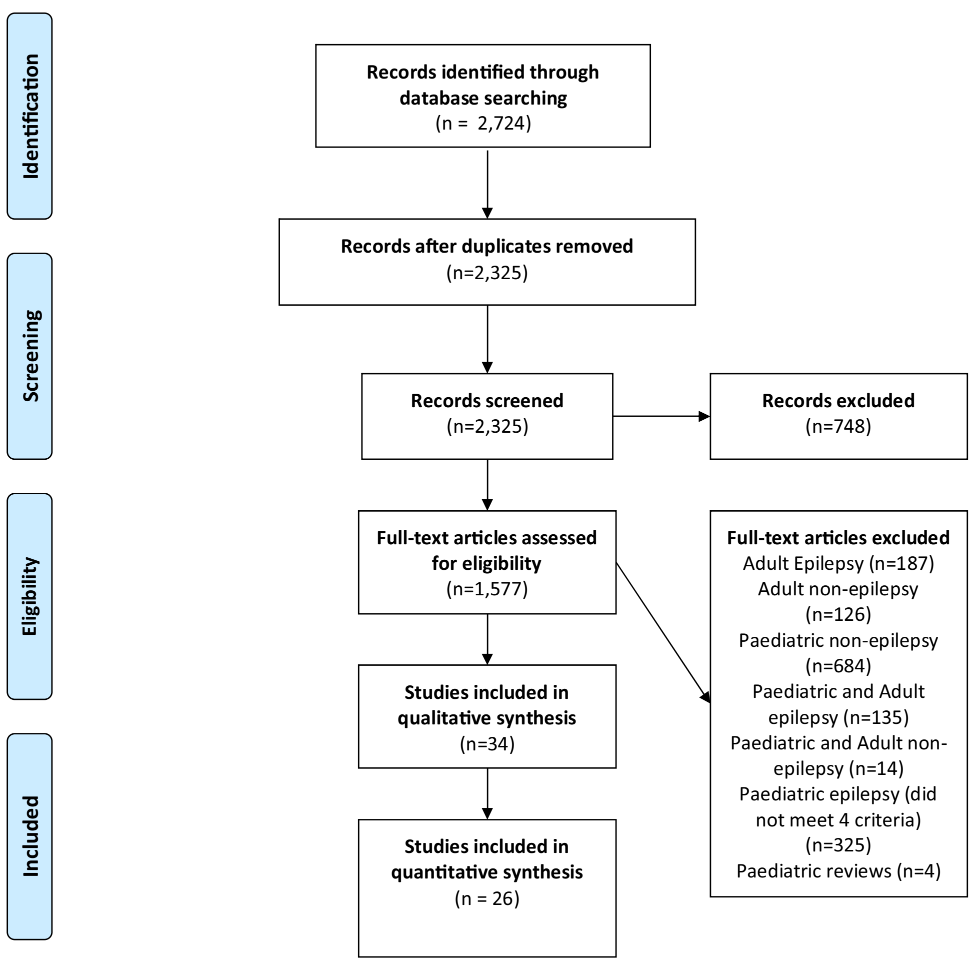

Fig. 1. PRISMA Diagram.